

*In Biography
Envelope*

Extract from Nature , June 20, 1942 p. 692

PROF. E.D. ADRIAN, O.M., F.R.S

The recognition of the value of the work of Prof, E.D.Adrian to science by the award of the Order of Merit will be a source of great pleasure to his colleagues and students throughout the world. The advance in our knowledge of the working of the nervous system that has taken place in the last twenty years owes much to his long series of researches into the nature of the fundamental processes in nerve cells. As research in clinical neurology is able to make full use of this knowledge, further advances may also spring from his work, but this application must, of necessity, take a long time to reach fruition. Prof. Adrian's work on nerve and muscle, in association with Keith Lucas, started before the War of 1914-18; during that War he worked in clinical neurology, which gave him a wide experience and interest in neurology as well as electrophysiology. During the War of 1914-18 Keith Lucas and Adrian had discussed the new possibilities opened up by the thermionic valve, of investigating the electrical activity of the nervous system in detail. After Lucas's death, Adrian succeeded in realizing these possibilities, and in 1924 started the series of researches on the activity of single nerve fibres which in the next ten years were to yield such a rich harvest of new knowledge of the action of the sense organs and of reflex activity. As technical advances became possible these were adopted to refine the method, and his laboratory became the centre of research in electrophysiology to which research workers went from all over the world to learn these methods. The focus of work gradually moved from the investigation of the electrical activity of the peripheral nerve fibres to that of nerve cells and synaptic regions of the central nervous system.

were given, and next day 8 oz. of urine was passed; after that she soon became normal again. Her jaundice was very definite, and her serum was icteric in appearance, with an indirect positive van den Bergh reaction. Her urine was rather dark, but was not examined spectroscopically for methaemoglobin. For about 48 hours her condition gave rise to anxiety.

Discussion

According to the information available, cross-matching before transfusion had shown no incompatibility. The result was, however, different when we had the opportunity of repeating the examination eight days after transfusion. It was beyond doubt that both the patient's and the donor's blood belonged to Group O. The only uncommon phenomenon on this re-examination was the agglutination of the donor's corpuscles by the patient's serum. The agglutinating action of the patient's serum on the donor's corpuscles was titrated by mixing equal amounts of serum dilutions and of an approximately 1% suspension of the donor's corpuscles; the result was noteworthy in two respects: (1) the titre of the irregular iso-agglutinin was rather high—1:64 at room temperature; and (2) the titre was increased to 1:128 when the tubes were kept in the incubator at 37° C.

Examination of other blood samples belonging to Group O showed that many corpuscles were agglutinated by the patient's serum, though in different degree. The serum yielded marked agglutination with corpuscles of 87 (75%) out of 116 Group O persons. On the other hand, 44 other sera did not agglutinate the donor's corpuscles or such O corpuscles as were agglutinated by the patient's serum. The conclusion must be drawn, therefore, that the uncommon behaviour is due to a peculiar property of the patient's serum. In these circumstances the possibility had to be considered whether the patient and the donor belonged to different types within the M-N system, although anti-M and anti-N antibodies are hardly ever present in human serum and are usually not produced by iso-immunization in man. Actually the patient's and the donor's bloods belonged to different types, the patient's corpuscles containing the factor M, the donor's corpuscles the factor N. The use of anti-M and anti-N sera as well as tests with the patient's serum showed, however, that there was no agreement either between the action of the patient's and anti-M serum or between that of the patient's serum and anti-N serum. The possibility that the accident following transfusion and the presence of irregular iso-agglutinins in the patient's serum was caused by the interference of anti-N agglutinins may therefore be excluded.

The iso-agglutinin observed is different from many irregular iso-agglutinins in the fact that it acts in the warmth at least as strongly as in the cold. While other agglutinogens, apart from those characterizing the A-B and the M-N system, share the widespread distribution in human blood with the agglutinin observed by us, they have hardly ever caused a severe reaction after transfusion. In the older literature, however, observations are recorded which indicate that irregular agglutinogens may play an important part in this respect. References to these are given by Wiener (1939). A case reported by Zacho (1936) may be mentioned because of the impressive similarity to our observations. It concerned a pregnant woman who received some transfusions of homologous blood (Group A) and died after a severe haemolytic reaction following on transfusion. Cross-matching tests, made after the accident, showed that the patient's serum agglutinated the corpuscles of two of

Wiener (1941), antisera are obtained which after absorption with selected human bloods or even after simple dilution act only on human blood corpuscles which contain the Rh factor. The difference between the percentage of Rh-positive samples and the agglutination of blood samples by the patient's serum in our case or in that reported by Zacho need not be of much significance, for it is understandable that the immune serum used by Landsteiner and Wiener has a greater activity than human sera. Moreover, the patient's serum was withdrawn in our case at different times up to six weeks after transfusion, and the agglutinating power decreased by degrees rather quickly. The calculated percentage in our examinations (75%) refers, however, to the total of all tests, so that it may be considered as an average.

According to the papers recently published by Wiener and Peters (1940), Wiener and Schaefer (1940), Levine and Katzin (1940), Levine, Katzin, and Burnham (1940, 1941), and Wiener (1941), the Rh factor is hereditary. When, therefore, the foetus has inherited the Rh factor from the father, and the mother has not this factor, iso-immunization of the mother may occur from the foetus *in utero*, so that anti-Rh antibodies are produced in the mother. They may, on the one hand, penetrate the placental barrier and in such a way induce erythroblastosis foetalis, as Levine, Katzin, and Burnham (1941) have assumed. On the other hand, their presence in the mother may be the reason that at the first transfusion accidents occurred which have been described especially in intra-partum or post-partum cases. In the same way it is understandable that reactions following repeated transfusion of homologous blood may happen when the patient is Rh-negative and the donor Rh-positive.

As in our case the severe reaction followed the first transfusion, it must be assumed that, if the irregular iso-agglutinins correspond to the Rh antibodies, the patient was immunized during pregnancy. Because of the heredity of the Rh factor the conclusion was reached that the patient's husband must be Rh-positive. Unfortunately the husband's blood was available only about six weeks after transfusion, at a time when the irregular iso-agglutinins of the patient's serum were already very much weaker. Nevertheless it was possible, by freezing the serum and using the layers at the bottom of the frozen serum—a method successfully utilized by O'Meara (1933) for concentrating iso-agglutinins—to obtain a concentrated fluid from the patient's serum which agglutinated the husband's blood corpuscles, also belonging to Group O, distinctly. In this way it could be shown that the iso-agglutinogens, the antibodies of which were in the patient's serum, were present in the husband's corpuscles. Thus it seems justifiable to assume that the irregular iso-agglutinins in the patient's serum may have been the consequence of an iso-immunization of the patient during pregnancy. The children's corpuscles, however, were not available for testing against the mother's serum.

Conclusion

It must be emphasized that the identity of the irregular iso-agglutinin observed in our case with the anti-Rh agglutinin has not been proved, because a known anti-Rh serum was not available for our examinations. Nevertheless, the activity of the agglutinin in the warmth, the frequency of the corresponding agglutinin among the population, and the fact that the irregular iso-agglutinin was detectable only after transfusion for a relatively short period and not on cross-matching beforehand, may favour assumption of interference by anti-Rh antibodies and Rh antigens. The peculiarities correspond to those referred to by the American authors, particularly by Wiener. On the other hand, the fact must be stressed that reactions caused by the interaction of Rh-positive blood and its antibodies are described only on repeated transfusion or in women who had recently given birth or had had a miscarriage or a stillbirth. Our patient had had children. It must be borne in mind, however, that the last birth occurred

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cases and in others might

The spread of interest in brain potentials in man is largely due to Adrian's work in this field; the implications of the discoveries in this field by Hans Berger were not generally realized and the discoveries lay dormant for ten years until Adrian re-investigated them, confirmed and extended Berger's work, and linked up his findings with general knowledge of the nervous system by animal experiments. Adrian's main interest has always been to discover the principles underlying all nervous structures as these apply throughout the animal kingdom, and the application of these to the nervous system of man. Thus his work on the electrical activity of the nerve ganglion of the water beetle assisted him in interpreting brain potentials in man; again, experiments on single motor nerve fibres in cats led to the investigation of voluntary control of human muscles in intact man by needle electrodes, and this method has become a valuable tool to the neurologist in investigating the nature of nervous diseases. Adrian's work owes much to his manual dexterity; he carries out all details of experiments himself and constructs much of his own apparatus. He encourages his students to work in the same way to the surprise of some visitors who expect to find a large staff of technical assistants. The success of this policy of close contact with experimental material is attested by the large volume of research carried out by students in his laboratory, and by schools founded abroad by physiologists trained in electro-physiological research in Cambridge. Since Prof. Adrian's work on individual nerve cells has been complementary to the researches of the Sherrington School on reflex action and the behaviour of large numbers of neurones, it is fitting that he should join Sir Charles Sherrington in the select company of those who have received the Order of Merit.

created. Every minute of the time of every medical man should be devoted to this task.

In these circumstances it is deplorable that the fear of a new Act, the fear of an unacceptable State Medical Service, or of any other drastic reorganization of medical service by the Government, should make it necessary for medical men to be urged, as they are being urged, to attend meetings and conferences, to initiate study circles, to issue memoranda, to spend time and thought, and to deflect to the study of post-war problems the energies which should be spent in the problems of the moment. The Prime Minister has given a lead as to the proper allocation of time to post-war planning. Other Ministers should follow that lead. Let the Ministry of Health concern itself with the present emergency and with that alone. Let us first win the war, and when our primary task is accomplished, then let us turn to replanning and to the more permanent improvement of medical service.

I may add that this is not a personal point of view alone. When it was presented to-day to a meeting of 200 medical practitioners, surgeons, and consultants in Liverpool it was received with acclamation and general approval.—I am, etc.,

Liverpool.

R. WATSON-JONES.

The Teaching of Anatomy

SIR,—The recent correspondence and your leading article serve to emphasize one significant fact. In spite of a great deal of criticism, constructive and otherwise, extending over a period of many years, the teaching of anatomy has not undergone any radical change. There seem to be two main reasons for this.

First, the question of "unnecessary topographical minutiae." The desire to eliminate these is frequently expressed, but as yet is only a desire. One of your correspondents says that "the anatomist of to-day attaches little value to detail." He may be right, but the current textbooks afford no indication of this. It is not surprising, therefore, that the student, on being confronted with the textbook recommended to him, concludes that detail is important and does his best to try and master it. The need for a fundamentally different type of textbook is urgent: not merely one modelled on the same lines as its predecessors of two or three generations ago, with some additional facts and a few x-ray plates thrown in, but one in which anatomists would have the courage of their convictions, and demonstrate to their students (and themselves) that they really meant what they said when they talked about discarding "unnecessary topographical minutiae." Prof. Wood Jones (March 14) is, of course, quite right when he emphasizes the difficulty of securing general agreement as to what minutiae are necessary or not. But are anatomists to allow this difficulty to deter them from ever making the attempt to give concrete expression to what is otherwise destined to remain merely a pious hope? First attempts might meet with abundant criticism and only partial success, but failure to make the attempt is quite certain not to meet with any success whatever.

The second problem concerns the correlation of dissecting room and clinical work. This really involves two distinct stages, beginning with the application of dissecting room findings to the normal living body, followed by a comparison with deviations from the anatomical norm as they occur clinically. Most anatomists nowadays accept the principle that the study of anatomy in the dissecting room is not an end in itself, but merely an intermediate stage leading to the study of the anatomy of the living. But it is one thing to state the principle, another to apply it effectively, and the ideal way of doing so has, in most cases, not been attained. Neither in terms of the time allotted to it nor of the relative importance assigned to it in examinations can it be said that the anatomy of the living subject is treated really seriously. The traditional surface anatomy lectures, in which a group of students look on while the lecturer draws coloured lines on a living model, are further proof of this.

The remedy? Primarily a real determination on the part of anatomists and clinicians to collaborate in translating principle

readily available—are obtained when the students use themselves as models. Within the scope of living anatomy would come such things as percussion and palpation of viscera, identification of muscles (with much of their attachments) and their actions, tendons, arteries, bone and joint movements, correlated throughout with the actual dissection. This is by no means an exhaustive list—examination of the ear-drum, retina, interior of the mouth, vocal cords, radiographic examination of the body, all come within the scope of living anatomy. The living anatomy classes, which can only be efficiently conducted with small groups of students, take up a great deal of time but are exceedingly worth while.

The collaboration of the clinician is needed in the second stage of the process—the provision of clinical material for the study of simple deviations from the anatomical norm. It is preferable that the "academic anatomist" with all his faults (*pace* Mr. Jessop, Feb. 21) should be responsible in large measure for first introducing the student to clinical material, since he is in the most favourable position for integrating clinical findings with those of the dissecting room. As Mr. Wilfrid Adams points out (Feb. 28), administrative difficulties increase if hospital and anatomy department are some distance apart; but with a little energy and good will this difficulty should not prove insurmountable.

One need hardly add that these observations apply to the ordinary medical student training to become a general practitioner. For higher qualifications different standards would be aimed at once the ordinary degree had been taken.—I am, etc.,

Bristol.

J. M. YOFFEY.

SIR,—It must be well over twenty-one years ago (nearer fifty, I think) that Lawson Tait asked in a lecture "What use has 'BODFI' ever been to one of you or anyone else?" Your leading article (March 21, p. 390) expands and answers the question. We stuff the innocent student's mind with "BODFI" and its congeners, few of which can ever benefit him or his patients when he becomes a specialist; in which case he will study the mysteries underlying them at the end of his student career instead of at the beginning, when he hardly knows chalk from cheese. It seems high time to get a move on in the direction indicated in your leader.—I am, etc.,

Ambleside.

J. PRICE WILLIAMS.

** Students and practitioners of to-day may not all be familiar with "BODFI," which was a classical "tip" to indicate the meanderings "backward, outward, downward, forward, and inward" of the middle cornua of the lateral ventricles of the brain.

Loss of Vitamin C in Cooking

SIR,—Evidence is accumulating of a vitamin C shortage among members of the Services and others fed at canteens, although they eat plenty of vegetables. The explanation is found in the faulty and destructive methods of cooking, and it is to be hoped that the opinion expressed in your leader (Feb. 14, p. 227), that saturation with vitamin C is not necessary for health, will not be used to minimize the need for a plentiful supply of vegetables and so to defend the methods of cooking at civic restaurants and school canteens under the control of the Ministry of Food. That such a danger exists will be seen from a reply received when the Ministry's attention was drawn to the "soda-boiling" of greens at its restaurants. Referring me to the paper issued by the Medical Research Council concerning the preservation of vitamins in cooking greens the Ministry goes on: "You will note that the paper states that the addition of an alkali hastens the destruction of the vitamins and does not necessarily destroy them all." The method of cooking vegetables for school dinners is even worse than this senseless use of soda in civic restaurants, for these dinners are cooked in the early hours of the morning (starting at 7 a.m.) and kept hot until after morning school. As "keeping hot" is perhaps the surest way of destroying vitamin C, these vegetables are treated as if one were aiming at the utmost destruction of the antiscorbutic vitamin.